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EXAMINER	
HAMA, JOANNE	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,142	KYRKANIDES, STEPHANOS	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13,14,16-74,76-83,87,89-92,134,135,138 and 142* is/are pending in the application.

4a) Of the above claim(s) *13,44-71,76-82 and 92-132* is/are withdrawn from consideration.

5)☒ Claim(s) *83* is/are allowed.

6)☒ Claim(s) *1-11,13,14,16-43,72-74,87,89-91,134 and 135* is/are rejected.

7)☒ Claim(s) *14,138 and 142* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/3/08,12/23/08,1/13/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of March 26, 2008 on February 9, 2009. Claim 1 is amended. Claims 12, 15, 75, 84-86, 88, 133, 136, 139-141, 143 are cancelled. Claims 44-71, 76-82, 92-132 are withdrawn.

It is noted that "Claims 84-86 (Canceled)" should be written separately from claim 83.

Claims 1-11, 13, 14, 16-43, 72-74, 83, 87, 89-91, 134, 135, 138, 142, drawn to a composition comprising an isolated nucleic acid comprising a Hex-alpha and Hex-beta sequence, and to a method of making said composition.

Information Disclosure Statement

Applicant filed Information Disclosure Statements (IDSes) on January 13, 2009, December 23, 2008, and April 3, 2008. The IDSes have been considered.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 6, 16-18, 25 are remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record, March 26, 2008.

Applicant's arguments filed February 9, 2009 have been fully considered but they are not persuasive.

Applicant indicates that the specification provides support for a chicken beta-actin/CMV fusion promoter and refers to Daly et al., 2001, Beattie et al., 2008, Klein et al., 2008, Song et al., 2001, Nguyen et al., 2008, and Tenenbaum et al., 2004 (Applicant's response, page 16). In response, this is not persuasive. Daly et al. teach a construct that comprises a CMV enhancer and a beta-actin promoter (Daly et al., Figure 1, legend). This is not a teaching of a promoter that is a hybrid CMV promoter and a beta-actin promoter (see claim 25, which depends on claim 18). With regard to Song et al., 2001, Song et al. teach a CMV enhancer and beta-actin promoter (Song et al., page 1300, 1st col., 1st parag. under hAAT expression in murine hepatocytes). With regard to the other citations (Beattie et al., 2008, Klein et al., 2008, Nguyen et al., 2008, and Tenenbaum et al., 2004), all these publications are after the time of filing and cannot be relied upon for support at the time of filing.

Thus, the claims remain rejected.

Claims 1, 4, 6, 16-18, 25, 26, 29, 30, 87, 89 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a composition comprising an isolated nucleic acid wherein the nucleic acid comprises a sequence encoding a HEX-alpha and a sequence encoding a Hex-beta,

wherein the HEX-beta and HEX-alpha form a dimer and wherein the dimer can catabolize GM2 gangliosidase,

does not reasonably provide enablement for

a) said composition comprising a promoter, wherein the promoter is a CMV-beta-actin hybrid,

b) said composition producing a HEXB product which cross-corrects and catabolizes GM2 gangliosides,

c) said composition comprising a cell specific promoter as set forth in SEQ ID NO. 69.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for reasons of record, March 26, 2008.

Applicant's arguments filed February 9, 2009 have been fully considered but they are not persuasive.

Applicant indicates that the specification provides examples of combination promoters (Applicant's response, page 16). In response, as discussed above, this is not persuasive. Daly et al., 2001 and Song et al., 2001, teach a CMV enhancer and a beta-actin promoter, but do not teach a promoter that is a hybrid between a CMV promoter and a beta-actin promoter. The rejection as it applies to this issue remains.

With regard to the rejection of the claims being drawn to HEXB product cross-correcting and catabolizing GM2 gangliosides (claims 29, 30), Applicant indicates that the claims meet the limitation of catabolizing GM2 and refers to paragraph 62 of the

specification. Applicant indicates that "wherein the HEX-beta and HEX-alpha can form a dimer, and wherein the dimer can catabolize gangiloside *in vivo*," makes clear that the activity being discussed is activity by the dimer which must be a HEXA and not a HEXB dimer (Applicant's response, page 17). In response, this is not persuasive. Applicant correctly points out that paragraph 62 teaches that HEXA (the complex comprising a heterodimer of Hex-alpha and Hex-beta) has the ability to catabolize GM2. However, nothing in the specification teaches that HEXB (the complex comprising a homodimer of Hex-beta) has any GM2 catabolic activity. Claims 29 and 30 (which depend on claim 26) are drawn a HEXB dimer that has activities of cross-correcting and catabolizing GM2. Paragraph 62 teaches that "HEXB" is a Hex-beta homodimer. Chavany and Jendoubi, 1998, Molecular Medicine Today, 4: 158-165 teach that HexB is a homodimer of beta subunits and has similar substrate specificity to HexA with the key exception that it does not hydrolyze GM2 (Chavany and Jendoubi, page 158, 2nd col., 1st parag.). As such, neither the specification nor the art provide guidance that HEXB (the homodimer of Hex-beta proteins) has any GM2 catabolic activity. The rejection as it applies to this issue remains.

Applicant indicates that claim 88 has been cancelled and the rejection regarding SEQ ID NO. 69 and the NSE promoter are moot (Applicant's response, page 17). In response, this is not persuasive. Claim 89 is drawn to a promoter that comprises SEQ ID NO. 69. As indicated in the Office Action, SEQ ID NO. 69 comprises the sequence of the NSE promoter and part of cloning vector and it is unclear how an artisan

transcribes a gene of interest if the gene of interest is cloned after the cloning vector in SEQ ID NO. 69. The rejection as it applies to this issue remains.

Thus, the claims remain rejected.

It is noted that the rejection of claim 88 is withdrawn as the claim is cancelled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 89 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 89 depends on claim 88, which has been cancelled. In the interest of compact prosecution, claim 89 has been interpreted to depend on clam 87.

Claim 22 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record, March 26, 2008.

Applicant's arguments filed February 9, 2009 have been fully considered but they are not persuasive.

Applicant indicates that claim 22 has been amended to depend from claim 20 (Applicant's response, page 17). In response, no amendment to claim 22 has been made. The rejection of claim 20 remains.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11,13, 16-21, 23, 24, 26-28, 31-39, 43, 72-74, 134, 135 are remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brown and Mahuran, 1993, American Journal of Human Genetics, 53: 497-508, in view of Li and Li, 2001, International Congress Series, 1223: 3-15, Rossi et al., 1998, Nature Genetics, 20: 389-393, Kim et al., 1992, Molecular and Cellular Biology, 12: 3636-3643, Proia, 1988, PNAS, USA, 85: 1883-1887, Myerowitz et al., 1985, PNAS, USA, 82: 7830-7834, Patapoutian et al., WO 02/101045 A2, published December 19, 2002, Hobbs [online], 1997 [retrieved on 2008-03-02]. Retrieved from the Internet:< URL: http://www.ncbi.nlm.nih.gov/entrez/viewer.fcgi?cmd=Retrieve&db=Nucleotide&list_uids=2329859&dopt=GenBank&WebEnv=0npmzO46M-ZDooSIRrzuukhPw99uI5bvKx98CayPdO_uLYe5w4_-6eC9cd-KucPViMuvowjZ0gwTJT%40256362576FC165A0_0107SID&WebEnvRq=1>, pages 1-3, Hennighausen and Fleckenstein, 1986, EMBO Journal, 5: 1367-1371, Kost et al., 1983, Nucleic Acids Research, 11: 8287-8301, Kistner et al., 1996, PNAS, USA, 93: 10933-10938, Sauer, 1998, Methods, 14: 381-392, Banerjee et al., 1994, The Journal of Biological Chemistry, 269: 4819-4826, for reasons of record, March 26, 2008.

Applicant's arguments filed February 9, 2009 have been fully considered but they are not persuasive.

Applicant indicates that Brown and Mahuran disclose transfection of a mutant HEXA gene producing a mutant alpha subunit producing mutant HexA activity in Cos cells. Brown does not disclose expression of HEXA and HEXB on a single plasmid to produce functional HexA product in vivo. With respect to obviousness, this is important because the Cos cell system used by Brown does not have any native Hex-alpha or any mutant Hex-alpha in a system in which there is no competing Hex-alpha to disrupt the transfected produced HexA or HexB (Applicant's response, page 20). With regard to Applicant indicating that the Cos cell system used by Brown does not have native Hex-alpha nor mutant Hex-alpha in vivo, nothing in the claims require that the system be carried out in vivo, nor that the transfected cells be expressing any native Hex-alpha or Hex-beta. The claims are drawn to a product that is an expression vector that comprises the coding sequences of Hex-alpha and Hex-beta, regardless of intended use of the product. Brown and Mahuran teach wild type and mutant forms of Hex-alpha and Hex-beta in separate plasmids. Kim et al. teach that at the time of filing, that expression systems (i.e., vector) that expressed more than one transgene of interest were known. As such, an artisan would have combined Brown and Mahuran and Kim et al. in order to arrive at one expression system that expressed two transgenes of interest. With regard to Applicant indicating that there is no competing Hex-alpha to disrupt the transfected produced HexA or HexB, the claims do not require any specific biological activity. All that is required is an expression system that has a particular structure. The combination of Brown and Mahuran and Kim et al. give guidance to an artisan to arrive at this expression system.

Applicant indicates that neither Kim et al. nor Brown and Mahuran provides a motivation to combine Hex-alpha and Hex-beta into a single vector with an IRES sequence such that the vectors can be expressed in the brain. (Applicant's response, page 21). In response, there is no requirement in the claims that the expression system be expressed in brain. The only requirement of the claims is that they comprise specific elements. There is no requirement that the claimed product be used in specific applications. Brown and Mahuran and Kim et al. provide guidance to arrive at an expression system that comprises the claimed elements. Applicant indicates that Brown does not provide any teaching that would render the claims obvious as Brown does not teach the expression or production of both Hex-alpha and Hex-beta from a bicistronic gene. This would be required to make claims 1-41, 72-75, 83-91 obvious (Applicant's response, pages 21-22). In response, this is not perusasive. Had Brown taught a bicistronic expression vector comprising the coding regions of Hex-alpha and Hex-beta, this would render the claims anticipated and the claims would have been rejected under 102. However, because the Examiner has indicated that Brown does not teach bicistronic constructs and has relied upon Kim et al. for teaching bicistronic expression systems, the rejection is a 103.

Applicant indicates that Kim et al. do not teach anything about Hex-alpha and Hex-beta. Kim et al. do no teach anything about using a lentilviral vector for transduce the cells or about the amelioration of Tay Sachs or Sandoff's disease (Applicant's response, page 22). In response, this is not persuasive. Kim et al. was not applied as a 102 rejection. Rather, it was used in a 103 rejection in combination with Brown and

Mahuran who teach Hex-alpha and Hex-beta. Kim et al. was used to teach that expression systems that express more than one transgene of interest were known. It would have been obvious to take the teachings of Brown, who teach Hex-alpha and Hex-beta and to put those genes into the bicistronic system of Kim et al. in order to arrive at a system that expressed two transgenes from one vector. One advantage of this is that an artisan would need to transfect only one transgene, rather than two independent expression vectors, which has the problem of one, but not the other expression vector transducing the cell. It is noted that Kim et al. teach another advantage of using a system that expresses multiple genes from one vector is that it allows temporally and spatially coordinated expression of two different genes driven by a single promoter in a single cell (Kim et al., abstract). With regard to Applicant indicating that there is no teaching of lentiviral vectors, it is noted that the Examiner relied upon Chavany and Jendoubi for this teaching (Office Action, March 26, 2008, pages 13-14).

Applicant summarize the Office Action's rejection as: 1) the individual pieces of the claimed nucleic acids were known (p. 8 and 9 of the Office Action) (except for the FIV vector, in this rejection), 2) Brown showed that two (non FIV) vectors could infect COS cells (p. 8, of the Office Action), and 3) Kim et al. allegedly teach the expression of two proteins from a bicistronic gene using an IRES sequence (p. 9, of the Office Action) with the conclusion being,

> "It would have been obvious to one of ordinary skill in the art to take Kim et al's teaching of using an IRES in an expression vector such that [Hex A] HexA and [Hex B] HexB can be expressed from one vector. (p. 9, of the Office Action).

The Examiner has attempted to combine 14 references to arrive at the present rejections, and has not pointed to a single spot in any of the references where there was even a hint, much less a suggestion or motivation, to arrive at the claimed nucleic acids (Applicant's response, page 22). In response, the motivation to combine the references was taught by Kim et al. Kim et al. teach the advantage of using a system that expresses multiple genes from one vector is that it allows temporally and spatially coordinated expression of two different genes driven by a single promoter in a single cell (Kim et al., abstract). Further, as indicated by the Examiner, an artisan would have combined Brown and Mahuran with Kim et al. in order to arrive at a system that expressed multiple transgenes from one vector than from individual vectors because one vector minimizes the chance that a cell would be transfected with one, and not both expression vectors. With regard to Applicant indicating that there is no teaching of lentiviral vector, nothing in claim 1 requires a lentiviral vector. In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). It is noted that the rejection at hand is based primarily on Brown and Mahoran and Kim et al. The other references were used to reject the dependent claims that further limit claim 1.

Applicant indicates that the Examiner has provided no evidence of reasonable expectation of success that the claimed compositions would produce beta-hexamindase (Applicant's response, page 23). In response, this is not persuasive. The claims are

drawn to an expression system that comprises the Hex-alpha and Hex-beta genes. The combination of Brown and Mahuran and Kim et al. lead an artisan to make an expression system that expresses HexA and HexB proteins from the same vector. There is reasonable expectation of success that an artisan would have made the expression vector because Kim et al. teach that the expression system express two or more transgenes spatially and temporally in one cell.

Applicant indicates a secondary consideration. Applicant indicates that there is teaching away from the claimed invention. Applicant indicates that previous attempts to provide HEXA and HEXB in vivo on separate plasmids, much less single plasmids were unsuccessful. Applicant refers to teachings of Guidotti et al., 1999. Applicant indicates that the Hex-alpha and Hex-beta subunits must be expressed properly and soichiometrically associate and form a functional beta-hexoaminidase enzyme (Applicant's response, pages 23-24). In response, this is not persuasive. As indicated above, there is no specific requirement that the claimed expression system be used in gene therapy. An artisan would have made the construct to express in Cos cells, like the system taught by Brown and Mahuran, in order to measure the amount of heterodimer formation of various combinations of HexA and HexB wild type and mutant proteins. To simplify the system of transfecting two expression vectors, an artisan would have taken the teachings of Kim et al. to arrive at one expression vector that comprised the coding sequences of HexA and HexB proteins. There was reasonable expectation of success of making the vector because Kim et al. teach that two distinct genes could be expressed in their system.

With regard to the issues of supporting references, Applicant indicates that rejection indicates that the orientation of HexA and HexB around the IRES is a "matter of design." Applicant indicates that orientation plays a critical role in the stoichiometry of production of Hex-A and Hex-B (Applicant's response, page 24). In response, as discussed above, there is no requirement of stoichiometry of HexA and HexB production in the claims. The claims are drawn to a product, wherein the product is an expression system that expresses two transgenes of interest (Hex-alpha and Hex-beta).

With regard to the rejection relying on the supporting references that reject the dependent claims (Kim et al., for using a second IRES and a reporter gene, Brown and Mahuran for the use of an SV40 promoter, Henninghausen and Fleckenstein for the use of a CMV promoter, Kost for the use of a beta-actin promoter, Kistener et al. for the teaching of inducible promoters, Sauer to teach recombinase sites, Banerjee for teaching stable integration into a genome), Applicant indicates that there has been no attempt to link these references with the base references in the context of the present claims. Just because the elements are present, a hindsight rejection, asserting that it would have been obvious to combine these elements, does not provide a prima facie case of obviousness. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As indicated above and in the Office Action of March 26, 2008, the art provides guidance for combining the teachings of Brown and Mahuran and Kim et al. With regard to the teachings of the dependent claims, wherein the claims are drawn to specific embodiments, the art teach that these embodiments were known and that these embodiments provide advantages and/or flexibility to an expression system. Thus, an artisan would have taken these teachings and adapted them to Brown and Mahuran and Kim et al.

Thus, the claims remain rejected.

Claims 1, 4, 6, 39-42, 87, 90, 91 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Brown and Mahuran, 1993, American Journal of Human Genetics, 53: 497-508, in view of Li and Li, 2001, International Congress Series, 1223: 3-15, Kim et al., 1992, Molecular and Cellular Biology, 12: 3636-3643, Chavany and Jendoubi, 1998, Molecular Medicine Today, 4: 158-165, Schuette et al., 1999, Biol. Chem. 380: 759-766, Litchtler et al., 1989, The Journal of Biological Chemistry, 264: 3072-3077, Klimatcheva et al., 1999, Frontiers in Bioscience, 4: 481-496, for reasons of record, March 26, 2008.

Applicant's arguments filed February 9, 2009 have been fully considered but they are not persuasive.

Applicant indicates that there has been no attempt to link the references together with the base references in context of the present claims. Just because the elements

are present, a hindsight rejection was made. Applicant indicates that there has only been assertion that it would have been obvious to combine these elements and no reasonable expectation of success (Applicant's response, page 26). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In addition to this, as discussed above, there would have been motivation to make an expression system that expresses HexA and HexB protein from one vector. Guidance was provided by Brown and Mahuran for teaching expression of HexA and HexB wild type proteins and mutant proteins in cell culture, to determine the effects of mutants on heterodimer formation, and by Kim et al. for teaching the benefits of expressing multiple transgenes from one expression vector. With regard to the other supporting references, the supporting references were used to address the claims that are drawn to specific embodiments of the expression system. With regard to using cell-specific promoters, the art teaches that defects in GM2 catabolism can affect specific tissues (e.g. brain and skin), that an artisan has the flexibility of expressing Hex-alpha and Hex-beta by using either an ubiquitous or a skin-specific promoter in order to arrive at a system that expresses Hex-alpha and Hex-beta in neurons or skin. Again, it is reiterated that the claims are drawn to an expression

system that comprises the Hex-alpha and Hex-beta genes, regardless of intended use and that the rejection is based on the structure of the expression system being obvious. There is no limitation to the structure that the system can be used for gene therapy. The system can be use in vitro and can be used to make a cell culture model of defective GM2 catabolism or a cell culture model of treating defective GM2 catabolism.

Thus, the claims remain rejected.

Conclusion

Claims 14, 138, 142 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim 83 is allowable.

Claims 1-11, 13, 14, 16-43, 72-74, 87, 89-91, 134 and 135 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Mondays, Tuesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Primary Examiner
Art Unit 1632